

REMARKS

Reconsideration of the subject application in view of the preceding amendments and the following remarks is respectfully requested.

Claims 55-58, 61-79, 82, 85, 88-94 and 97 remain pending in this application. In this amendment, Claim 55 has been amended to point with particularity what was believed to be inherently claimed and improve the clarity of the claim language. No new matter has been added to the subject application by this amendment, nor have any new issues been raised.

The Rejections Asserted in the Office Action

In the outstanding Office Action, Claims 55-58, 61-79, 82, 85, 88-94 and 97 were rejected under 35 U.S.C. §112, second paragraph, and again rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over U.S. Pat. No. 5,362,497 to Yamada et al., in view of U.S. Pat. No. 4,299,828 to Wang et al. and U.S. Pat No. 4,552,872 to Cooper.

Response by Applicant

Applicants traverse the Examiner's rejections primarily because of the reasons set forth herein below. Applicants believe the claims as examined were directed to subject matter which was neither disclosed nor suggested by the cited references in the office action. By this amendment, Applicants have amended the claims of the instant application in an effort to advance prosecution, among other things, but not in acquiescence of any rejection thereto. Applicants respectfully submit that the claims as now presented are also directed to subject matter which is neither disclosed nor suggested by the cited references in the office action.

Furthermore, Applicants believe these claims are now in condition for allowance. For illustrative purposes, Applicants have addressed the rejections in the outstanding office action as if the rejections had been asserted against the claims in their newly amended form.

Claim Rejection – 35 U.S.C. § 112

In the outstanding Office Action, the Examiner states the following as support for the outstanding 112 rejection:

Claim 55 is drawn to a composition comprising a) a solvent, which comprising unsaturated fatty alcohol and propylene glycol; and c) a plasticizing agent, which would read on the unsaturated fatty alcohols, or propylene glycol recited in a) (see, the specification, page 8, lines 22-31). The double inclusion of such elements renders the claim indefinite as to the particular amounts of a) and c) recited in the claimed composition. One of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

In addition to previous arguments, Applicants respectfully submit that there is no U.S. patent rule which requires that compounds must fall only within one element of a claim. The present invention as presently claimed is directed to novel solid, dermatological compositions, and methods of making and using the same which incorporate well known compounds for use as a solvent or a plasticizing agent. It should be readily apparent that the present invention is not directed to novel solvents or plasticizing agents.

The use of certain compounds as solvents or plasticizing agents is well known, and therefore, from reading and comprehending the present specification and based on general knowledge in the art, Applicants contend that one skilled in the art would easily understand that some compounds that may be suitable solvents would also be a suitable plasticizing agent and therefore can be used as a solvent or as a plasticizing agent in the claimed invention. Applicants

further contend that one skilled in the art will easily be able to recognize and use compounds as solvents and plasticizing agents within the scope of the present claims.

Clearly, even though the same compound may be suitable for use as a solvent or as a plasticizing agent, this claim does not contain a "double inclusion" of the same element because the two claimed elements themselves are not the same. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claim Rejection – 35 U.S.C. § 103

In combining Yamada, Cooper and Wang to formulate the outstanding 103 rejection, the Examiner has argued:

A person of ordinary skill in the art would have been motivated to modify the composition of Yamada to make a corticosteroid containing topical composition employing oleyl alcohol as the fat soluble enhancer and propylene glycol as the water soluble enhancer with the particular amounts claimed herein because both are known to be useful to enhance the absorption of the active ingredients and the amounts of such ingredients herein is encompassed by scope taught by the prior art. The employment of wax and plasticizer to render the final product certain properties (such as those required for stick formulation) is seen to be within the skill of artisan. The optimization of the amounts of each known ingredient in the composition is considered within the skill of the artisan, absent evidence to the contrary.

In addition to previous arguments, Applicants contend that the Examiner has not satisfied the burden necessary for establishing a *prima facie* case of obviousness, as alleged in the outstanding office action.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, to establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The requisite motivation does not exist to combine the cited references in a manner which renders the claimed invention obvious

The Examiner has not provided the requisite motivation for combining the cited references in a manner which anticipates the instant invention as claimed. The allegation that both oleyl alcohol and propylene glycol are known to be useful to enhance the absorption of the active ingredients does not provide motivation from the cited references or elsewhere for making a composition as claimed.

In particular, Claim 55 is directed to a solid, dermatological composition comprising a biologically active agent dissolved in a homogeneous carrier system, wherein the carrier system includes:

- a) a solvent for said active agent, comprising 20 to 85% by weight of an unsaturated fatty acid alcohol in combination with an alkylene glycol, said fatty acid alcohol being selected from oleyl alcohol, ricinolyl alcohol, linolyl alcohol and/or linolenyl alcohol, and said alkylene glycol being selected from propylene glycol and/or dipropylene glycol, the alkylene glycol being present in an amount of more than 12% by weight to provide for mutual dissolution of said active agent;

- b) a viscosity enhancing agent for imparting a solid consistency to the composition which comprises 15 to 55% by weight of a waxy substance; and
- c) a plasticizing agent which comprises 2 to 30% by weight of a plasticizing oil; all percentages being based on the total weight of the carrier system.

In rejecting the Applicants invention, the Examiner has failed to examine the claimed invention as a whole in comparison to the cited references. In determining the differences between the prior art and the claims, the question under section 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983);

Although the rationale to modify or combine the prior art does not have to be expressly stated in the prior art, a statement that modifications of the prior art to meet the claimed invention would have been within the ordinary skill of the art at the time the claimed invention was made because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993).

In asserting this rejection, the Examiner has relied upon what was allegedly known to one skilled in the art, and not on an objective reason for making a combination as claimed by Applicants. Furthermore, the Examiner has not based the obviousness argument on what is claimed by Applicants as a whole. Rather, the Examiner has improperly asserted an obviousness rejection based on only two elements of the claimed invention and not the claimed invention as a whole. The Examiner asserts that "the employment of wax and plasticizer to render the final

product certain properties (such as those required for stick formulation) is seen to been [sic] within the skill of artisan," yet provides no proof from the cited references or elsewhere. Applicants contends that the Examiner has not based this outstanding obviousness rejection on the invention as a whole as claimed, and instead has made improper assertions without evidence, relying solely and impermissibly on what was supposedly known to one skilled in the art.

There is no reasonable expectation of success to modify the cited references

Second, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

Applicants respectfully maintain their position that Yamada et al. is irrelevant to the presently claimed invention and, in fact, teaches away from the presently claimed invention. Applicants contend that one skilled in the art would not foresee a reasonable expectation of success to modify Yamada to make the claimed invention. Yamada et al. seek to avoid separation of a transdermal therapeutic composition, comprising a water-soluble and a lipid-soluble enhancer from an adhesive via the use of a water absorbent resin. See col. 2, lines 25-35. Yamada et al. explicitly state that the use of alkylene glycol and fatty acids or alcohols are incompatible (col. 1, lines 6266). The presently claimed invention solves the incompatibility problem via specific mixtures of solvents to create a one-phase system while the solution to the problem in Yamada et al, is to utilize a superabsorbent polymer. This superabsorbent polymer is a critical element of the disclosure of Yamada et al. Applicants maintain that the skilled artisan would not obviously appreciate that enhanced homogeneity and penetration could be generated by a formulation that does not contain adhesives and superabsorbing polymers such as those

discussed by Yamada et al. Yamada et al. do no provide an enabling disclosure for the presently claimed invention, i.e., Yamada et al. indicate that the problems of the prior art are overcome only with the use of the superabsorbing polymer. Thus, there is no motivation to use a composition of Yamada et al. *sans* the adhesives and superabsorbing polymers because Yamada et al. specifically highlight the problems with such a composition. In fact, such lack of motivation highlights the surprising nature of the presently claimed invention, which further supports a finding of non-obviousness.

Further, Applicants respectfully submit that the composition of Yamada et al. is intended for transdermal delivery of a therapeutic composition in order to produce the intended systemic effect (col. 1, lines 19-23 *et seq.*), while Applicants' claimed invention is directed toward the local delivery of the therapeutic ingredient to the skin. Indeed, Yamada et al. seek to achieve a pharmacologically active concentration in the bloodstream. Col. 1, lines 26-33. Applicants point to the extensive listing of systemic drugs in Yamada et al. in support of this. Col. 2, line 47 through Col. 3, line 25.

The Examiner argues that Cooper et al. teach the inclusion of a wax to impart the stiffness to the composition. Applicants acknowledge that Cooper discusses the use of wax in a composition. However, the Examiner ignores the express limitation of Cooper et al. on the amount of wax to be used in the composition. Col. 10, 1. 40-42, Cooper et al. state that waxes "are capable of significantly interfering with the penetration enhancing abilities of the present invention. " Cooper et al. discuss the use of compositions for local delivery and for systemic delivery. Col. 1, 1. 37-41. Cooper et al. state, "a vehicle system which increases both the level and speed of penetration of the steroid through the skin would be more efficient in the treatment of localized conditions and, more importantly, would greatly increase the chances of making

systemic treatment by topical application viable. " Col. 2, 1. 50-55. However, in discussing waxy components, Cooper et al. conclude that, "while a certain level of such ingredients can be tolerated in a system which is otherwise particularly effective, in a preferred embodiment of the invention such ingredients are limited to less than about 10 % and preferably less than 5 %. " (col. 10, 1. 49-54). Because, as discussed above, Yamada et al. is directed to the systemic delivery of active ingredients, one skilled in the art would not be motivated to use the high percentage of wax as presently claimed, as such a choice would reduce penetration of the active ingredients.

The Examiner chooses to ignore this inconsistency by alleging that Wang teaches an amount of wax of 10-40% and suggests that unexpected results are necessary. Office Action, page 4. Applicants respectfully submit that the Examiner has erred by simply picking and choosing whichever elements of each reference support his argument and ignoring those that teach away from the presently claimed invention. This is impermissible. "A prior art reference must be considered in its entirety, i.e., as a whole including portions that would lead away from the claimed invention." *See M.P. E.P. § 2141.02* citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), *cent denied*, 469 U.S. 851 (1984) (emphasis in original).

In contrast, independent Claim 55 requires "b) a viscosity enhancing agent for imparting a solid consistency to the composition which comprises 15 to 55 % by weight of a waxy substance." Thus, not only do Cooper et al. not disclose or suggest the specific limitations of the presently claimed invention, but Cooper et al. also expressly caution against using the very amounts the presently claimed invention advocates. Thus, Cooper et al. cannot be considered to

render the claimed invention obvious because it expressly teaches away from the particular limitations.

The Examiner has previously argued that Wang et al. disclose that steroid containing stick compositions can be manufactured and that the active ingredient is preferably dissolved in the formulation. However, the disclosures of Wang et al. or of Cooper et al. along with Yamada, fail to render the present invention obvious. Wang et al. disclose a composition that the present specification demonstrates does not work in practice. The examples in the instant specification (as recited in independent claim 55) clearly show that if the composition contains less than 12% of alkylene glycol, the pharmaceutical activity of the formulation is very low. This is not disclosed or suggested by Wang et al. In fact, Wang et al. state that the propylene glycol (used as an antimicrobial but that also acts as a penetration enhancer) is preferably from about 2 % to 10 % by weight and optimally from about 3 % to about 8 %. Col. 3, lines 17-22. Wang et al. note that a concentration of 6 % of propylene glycol kills 99.9 % of bacteria. Col. 3, lines 24-29. Again, the Examiner chooses to ignore the **express teachings** of the Wang et al. publication in order to support his argument of obviousness. In light of the fact that Wang et al. disclose that 6% polyethylene glycol kills nearly all bacteria and that the optimal range is one-quarter to two-thirds of the **minimal** amount required by the presently claimed invention, there is **no motivation** in the Wang et al. publication to use **at least** 12% of polyethylene glycol. Generally, one does not use more of an ingredient than is necessary. Therefore, one skilled in the art would not be motivated to use higher concentration of propylene glycol (such as that found in the Yamada et al. publication) in a steroid stick formulation based on the disclosure of Wang et al. Accordingly, the Wang et al. and Yamada et al. publications are incompatible.

Further, Wang et al. assert that waxes are preferably between about 10 to 40% and preferably about 15 to about 30% by weight. Col. 3, 1. 13-16. As noted above, Cooper et al. expressly seek to avoid such high amounts of wax. Thus, the Cooper et al. and Wang et al. publications are incompatible and cannot be combined to render the presently claimed invention obvious. Applicants respectfully submit that the Examiner has attempted to combine references which expressly contradict the selection of certain components, without considering these express contradictions.

The Examiner has provided no rational or compelling explanation for why one skilled in the art seeking to make a composition for systemic delivery as in Yamada et al. would turn to Wang et al. for guidance or, alternatively, when seeking to make a composition for local delivery as in Wang et al. would turn to Yamada et al.

Even if combined, the cited references do not teach the claimed invention

Finally, to establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

As described above, the Examiner has not satisfied the burden for establishing a *prima facie* case of obviousness for the above reasons. In particular, the Examiner points out no teaching in any of the cited references that anticipates the entire claimed invention. Furthermore, even if the cited references were combined, the combination would still not anticipate the claimed invention.

If one modifies the Yamada composition, a system where the polymer stabilization of a two phase enhancer system is highlighted, by adding viscosity enhancers and employing oleic alcohol, one merely obtains a two-phase matrix thickened by both waxes and a polymeric

emulsion stabilizer. The Examiner has provided no motivation to use the composition of Yamada et al. in the absence of the super water-absorbent polymer, the central focus of the Yamada et al. publication. Abiding by the disclosure of Cooper et al., one skilled in the art would believe that the presence of the waxes should be restricted to less than 10%. This resulting product will have very little, if anything, in common with the presently claimed invention.

Applicants respectfully submit that the three cited publications, Yamada et al., Cooper et al., and Wang et al., do not disclose all elements of the presently claimed invention, particularly the amounts of the different components of the composition, among other things. Indeed, as Applicants have shown above, the cited publications are incompatible with each other and teach away from the presently claimed invention. Moreover, in light of the teachings of Yamada et al., the results achieved with the presently claimed invention would be surprising to one skilled in the art. Thus, none of the cited publications, either alone or in combination, render the presently claimed invention obvious. Accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

In conclusion, Applicants contend that the claims are not indefinite and since the independent claims contain limitations which are neither taught nor suggested by the cited references, these claims are not rendered obvious. Furthermore, since the claims that depend from independent these claims provide further limitations, the dependent claims are also not rendered obvious by the cited references. Accordingly, it is submitted that all pending claims as presented herein are allowable, and withdrawal of all rejections are therefore respectfully requested.

If the Examiner believes that a personal or telephonic interview may facilitate resolution of any remaining matters, Applicant's representative may be contacted at the number indicated below.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Richard H. Newman", is written over a horizontal line.

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